REMARKS

The Office Action dated September 11, 2003 has been received and carefully noted. The preceding amendments and the following remarks are submitted as a full and complete response thereto. Applicants have cancelled claims 5, 17 and 20 without prejudice or disclaimer. Claims 1-4, 13, 14, 16, 18 and 19 have been amended. The details of the amendment of these claims are explained in the relevant sections below. No new matter has been added or no amendments which narrow the scope of any limitations of any claims has been made. Applicants also have added claims 21 and 22. Support for the new claim can be found throughout the specification, for example, lines 28-32, page 9 and Example 4 at page 40. Accordingly, claims 1-4, 6-16, 18, 19, 21 and 22 are pending and are submitted for consideration.

Amendments in the Drawings:

The clone name pC3-hedg55 was amended to pC3-hedg5-3. Support for the amendment can be found in the Brief Description for Figure 4A in the specification.

Amendments in the Sequence Listings:

Applicants note that SEQ ID NOs:14 and 29 are the same sequences and thus has deleted the redundant SEQ ID NO: 29 from the original Sequence Listings. Substitute Sequence Listings

are submitted, and entry thereof is respectfully requested. A substitute computer readable form of the Sequence Listings is also submitted. It is hereby certified that the content of the Sequence Listings recorded in the computer readable form is identical to the Sequence Listings in written paper and contains no new matter.

Objections to Sequence Listings

The Office Action has objected to the sequence listings for failing to comply with the sequence rules. In response, Applicants have amended the Brief Description for Figures 5A and 5B in the specification by correcting typographical errors in SEQ ID NO, and inserting new sequence identifiers.

Applicants have also corrected a typographical error in clone names appearing in the Brief Description for Figures 5A and 6 in the specification. Specifically, pC3-hedge5#4 have been revised to pC3-hedge5#3.4. Support for these amendments can be found in the corresponding figures which disclose the correct clone names.

Rejection of Claims 1-16, 18 and 19 under 35 USC § 112, second paragraph

The Office Action has rejected claims 1-16, 18 and 19 as allegedly indefinite for various reasons. Applicants respectfully traverse these rejections.

(1) "biologically active fragment"

The Office Action has objected to this term alleging that neither the specification nor the art provides an unambiguous definition for the term. Applicants note that "biologically active" is defined in the specification as "those forms, fragments, or domains of any HEDG-5 polypeptide which retain at least some of the biological and/or antigenic activities of any naturally occurring HEDG-5." (See lines 7-9, page 8). The specification clearly states that lysophosphotidic acid (LPA) is a functional agonist. Therefore, the current specification provides a clear definition of the term "biologically active fragment." Nonetheless, in an effort to advance the case towards allowance, Applicants have revised claims 1-4 to specify that the "biologically active fragment" is the one that is capable of activation by LPA.

(2) "stringent conditions"

The Office Action has also objected to the term "stringent conditions" in claim 6 as allegedly indefinite for the similar reason set forth in the above rejection. Contrary to the assertion in the Office Action, however, Applicants note that the specification provides detailed and extensive descriptions as to "stringent conditions" at pages 9 to 10. As stated in the specification, such hybridization conditions are described in the textbook, Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Press, 1989 so that one skilled in the art could readily determine "stringent conditions" to identify or detect identical or related nucleotide sequences. In addition, the nucleotide sequence in the group (d) of claim 6 is not only with specified hybridization conditions, but also with the sequence identity at least about 70%. Thus, Applicants respectfully submit that, given the detailed description of stringent

conditions combined with specific nucleotides as defined in claim 6, one skilled in the art would readily define the scope of the claim. For these reasons, Applicants respectfully request reconsideration and withdrawal of the objection to this term.

(3) Claims 16, 18 and 19

The Office Action has rejected claims 16, 18 and 19 as allegedly indefinite. The Office alleges that because binding is not the same as ligand or antagonist activity, a step for measuring binding activity renders these claims unclear as to if the claimed method is directed to identifying compounds that bind the EDG5 receptor, or compounds that have ligand or antagonist activity. While not acquiescing to the propriety of the rejection in the Office Action, Applicants have amended claims 16 and 18 to be directed to identifying compounds that bind to EDG5 (for claim 16) and that inhibit binding of ligands to EDG5 (for claim 18). Claim 19 has been revised to refer to ligand rather than agonist in view of the amendment of claim 18. Applicants respectfully submit that these amendments render moot the rejections of claim 16, 18 and 19.

(4) Others

In an effort to address the remaining rejections in the Office Action, Applicants have revised claim 3 to refer to a sequence identifier, SEQ ID NO: 22, in the sequence listing. Applicants have also revised claim 13 to recite "isolated" instead of "isolation," and claims 13 and 14 to refer to an amino acid sequence, SEQ ID NO: 14. These revisions of claims are made to address formal matters only and do not narrow the scope of any limitation of claims. In view

of the amendments of claims and foregoing remarks, Applicants respectfully request reconsideration and withdrawal of all of the indefiniteness rejections.

Rejection of Claims 1-16, 18 and 19 under 35 USC 101, first paragraph

The Office Action has rejected claims 1-16, 18 and 19 for lack of a credible, specific and substantial utility. Relying on Ancellin et al. and Vogler et al., the Office Action asserts that EDG-5 is one of at least three or five receptors that bind to sphingosine 1-phosphate (SPP), and SPP mediates a number of diverse biological responses. Based on this understanding, the Office Action alleges that since it is not known which biological response is induced by EDG-5, one skilled in the art would need to conduct significant further research to determine a specific utility for the claimed EDG-5. In addition, the Office Action contends that neither NF-kB activation via EDG-5 receptor activation nor binding of lysophospatidic acid (LPA) to EDG-5 would provide a specific utility because both of them lead to various biological responses. The Office Action further asserts that other utilities asserted in the specification are not considered to be credible, specific and substantial utilities. Applicants respectfully traverse the rejection.

As an initial matter, Applicants would like the Office's attention to the fact that the claimed EDG-5 receptor is a lysophospholipid (LPL) receptor which is activated by lysophosphatidic acid (LPA), not by sphingosine 1-phosphate (S1P)[1]. The specification clearly

[1] The Office Action uses a different abbreviations, SPP. For the sake of consistency, Applicants uses S1P in the response.

states that the HEDG-5 receptor identified in the present application recognizes LPA as a functional agonist. (See page 11)

Applicants believe that the confusion over a functional ligand for the claimed EDG-5 is largely attributed to different nomenclature of EDG receptors used by Applicants and in other literature. Applicants have used their own way of designating the numeric number of EDG receptors, EDG 1, 2 or 3, in the order of isolating the sequence for each receptor, which is different from nomenclature used in either Ancellin et al. or Volger et al. In fact, the EDG-5 receptor reported in these references is named EDG-4 according to the nomenclature used by Applicants. The claimed EDG-5 receptor is also called EDG-7 or LPA3, which is known to recognize LPA as a functional ligand. The sequence identity between the claimed EDG-5 receptor and the EDG-7 receptor disclosed in Bandoh et al., which is also pointed out in the Office Action, further confirms that the claimed EDG-5 receptor corresponds to the EDG-7 receptor in other literature. In an effort to clarifying any confusion caused by different nomenclature used by Applicants, Applicants provide the following nomenclature comparison table.[2]

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[2] This table modifies Table 1 reported in Chun *et al.*, "International Union of Pharmacology, XXXIV. Lysophospholipid Receptor Nomenclature," *Pharmacol Rev* 54:265-269 (2002) to include Applicants' nomenclature, a copy of which is appended hereto.

Nomenclature			
IUPHAR	Applicants	Agonist Ligand	Aliases in other references
LPA_1	Edg-2	LPA	Edg-2, vzg-1, rec1.3, GPR26, LP_{A1}
LPA_2	Edg-6	LPA	Edg-4, LP_{A2}
LPA_3	**Edg-5**	LPA	Edg-7, LP_{A3}
$S1P_1$	Edg-1	S1P	Edg-1, LP_{B1}
$S1P_2$	EDG-4	S1P	*Edg-5*, H218, AGR16, LP_{B2}
$S1P_3$	EDG-3	S1P	Edg-3, LP_{B3}
$S1P_4$	EDG-7	S1P	Edg-6, LP_{B4}
$S1P_5$	EDG-8	S1P	Edg-8, LP_{B5}

Applicants submit that the above understanding of nomenclature of EDG receptors further clarifies that the claimed EDG-5 receptor has LPA as a functional ligand. It is well-settled that an applicant needs to make only one credible assertion of specific utility for the claimed invention to satisfy the utility requirement. MPEP 2107.02-1. The specification discloses that EDG-2, EDG-5 and EDG-6 proved to be inflammatory LPA receptor subtypes of the EDG receptor family, which induces NF-kB when activated. In support of this finding, the specification incorporates by reference the U.S. provisional patent application (filed on November 25, 1998) and the corresponding PCT application (filed on December 30, 1998, WO 99/35259, a copy of which is enclosed herewith). (See page 38 of the specification).

According to WO 99/35259, EDG receptors are involved in an inflammatory response signaling pathway and an apoptotic signaling pathway. In particular, WO 99/35259 discloses that LPA will act as an agonist to EDG-2, EDG-5 and EDG-6 receptors, which leads to activation/production of NF-kB. Thus, WO 99/35259 discloses a specific correlation between NF-kB activation and the EDG receptors including EDG-5. That is, WO 99/35259 recognizes EDG-5 as a means for controlling NF-kB activation via binding to its agonist, LPA, thereby controlling apoptosis and inflammatory responses.

Furthermore, the specification of the present application provides more detailed observations on the function of the three EDG receptors. That is, the "Results" section in Example 3 (at page 39 of the specification) concludes that all three EDG receptors tested, including EDG-5, are capable of inducing inflammatory gene transcription through NF-kB. The specification further suggests that "the nucleotide sequence for HEDG-5 can be used in an assay to detect inflammation . . . associated with abnormal levels of HEDG-5 expression." (See page 16 of the specification).

Contrary to the examiner's assertion, therefore, the present invention provides a specific utility of the claimed invention by identifying the role of EDG-5 in modulating inflammatory response in relation to binding to LPA and activation of NF-kB. The finding of such a role of EDG-5 would be sufficient to enable one skilled in the art to recognize a substantial utility of EDG-5, for example, in treating inflammatory diseases such as rheumatoid arthritis or asthma. Therefore, Applicants respectfully submit that none of the references or assertions made in the

Office Action casts doubts on the utility of EDG-5 for controlling inflammatory response which is presented in the specification. Accordingly, reconsideration and withdrawal of the subject rejection are respectfully requested.

The Office Action has also rejected claims 1-16, 18 and 19. The non-enablement rejection is imposed on the basis of the lack of utility. Thus, Applicants respectfully request reconsideration and withdrawal of the non-enablement rejection for the same reasons set forth above.

Rejection of Claims 1-13, 15, 16, 18 and 19 under 35 U.S.C. 102(b)

The examiner has rejected claims 1-13, 15, 16, 18 and 19 as anticipated by Bandoh et al. (September 1999, J. Biol. Chem. 274:27776-27785). The rejection is premised on denial of priority claim of the present application for the lack of utility and enablement. As previously explained, the specification provides a specific, credible and substantial utility of the claimed invention, and is enabled. As such, because the specification meets both utility and enablement requirements, the present application is entitled to priority. In this regard, Applicants note that the Office misunderstood the priority document of the present application as PCT/CA98/01193. As clearly indicated in the Declaration filed December 4, 2000, the present application was filed to claim priority to two earlier U.S. applications, U.S. Patent Application Nos. 08/997,803 (filed on December 24, 1997) and 09/220,674 (filed on December 23, 1998). Since Bandoh et al. was published September 1999, after the later priority date, it cannot qualify as anticipatory reference

against the claimed invention. Accordingly, Applicants respectfully request withdrawal of this rejection.

Double Patenting Rejection

The Office Action has also rejected claims 1-16, 18 and 19 for alleged obviousness-type double patenting over claims 1-8 of U.S. Patent No. 6,057,126 ("the '126 patent"). While not acquiescing to the propriety of the rejection, Applicants will submit a Terminal Disclaimer, once allowable subject matter is determined.

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes. Reconsideration of the instant application, withdrawal of all rejections and early notice of allowance are respectfully requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

In the event that this paper is not timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fees for such an extension together with any additional fees may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By _____

Robert B. Murray
Registration No. 22,980

ROTHWELL FIGG ERNST & MANBECK, p.c.
1425 K Street, N.W., Suite 800
Washington, D.C. 20005
Telephone No.: 202-783-6040
Facsimile No.: 202-783-6031